=> fil zcaplus

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FILE COVERS 1907 - 10 May 2004 VOL 140 ISS 20
FILE LAST UPDATED: 9 May 2004 (20040509/ED)

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=> fil hcaplus

FILE 'HCAPLUS' ENTERED AT 08:17:17 ON 10 MAY 2004
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FILE COVERS 1907 - 10 May 2004 VOL 140 ISS 20
FILE LAST UPDATED: 9 May 2004 (20040509/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> fil biosis

FILE 'BIOSIS' ENTERED AT 08:17:22 ON 10 MAY 2004
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FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 6 May 2004 (20040506/ED)

FILE RELOADED: 19 October 2003.

=> fil stnguide

FILE 'STNGUIDE' ENTERED AT 08:17:27 ON 10 MAY 2004
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AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: May 7, 2004 (20040507/UP).

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L3 76 SEA FILE=HCAPLUS ABB=ON PLU=ON LIM/AU OR ("LIM J"/AU OR "LIM J A"/AU) OR ("LIM JULIANNE"/AU OR "LIM JULIE"/AU OR "LIM JULIE A"/AU OR "LIM JULIE ANNE"/AU)
L4 12 SEA FILE=HCAPLUS ABB=ON PLU=ON (L2 OR L3) AND ?PYRIMIDIN?
L5 9 SEA FILE=HCAPLUS ABB=ON PLU=ON L4 NOT (URANIUM? OR SPOT TEST? OR MERCAPTO?)/TI
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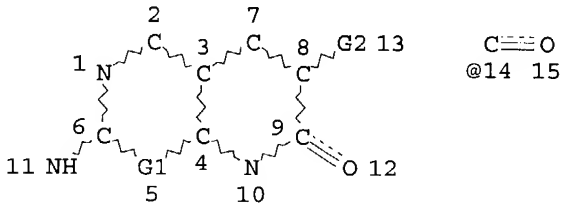

VAR G1=N/C
VAR G2=O/N/S/14
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 15

STEREO ATTRIBUTES: NONE
L11 (321) SEA FILE=REGISTRY SSS FUL L10
L12 6 SEA FILE=HCAPLUS ABB=ON PLU=ON L11
L13 7 SEA FILE=HCAPLUS ABB=ON PLU=ON L5 NOT L12

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L6 276 SEA FILE=BIOSIS ABB=ON PLU=ON GOLDSTEIN/AU OR "GOLDSTEIN D"/AU OR "GOLDSTEIN D M"/AU OR "GOLDSTEIN DAVID"/AU OR ("GOLDSTEIN DAVID M"/AU OR "GOLDSTEIN DAVID MICHAEL"/AU)
L7 173 SEA FILE=BIOSIS ABB=ON PLU=ON LIM/AU OR ("LIM J"/AU OR "LIM J A"/AU) OR ("LIM JULIANNE"/AU OR "LIM JULIE"/AU OR "LIM JULIE ANNE"/AU)
L9 4 SEA FILE=BIOSIS ABB=ON PLU=ON (L6 OR L7) AND ?PYRIMIDIN?

=> dup rem l13 l9

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FILE 'HCAPLUS' ENTERED AT 08:18:02 ON 10 MAY 2004
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FILE 'BIOSIS' ENTERED AT 08:18:02 ON 10 MAY 2004
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PROCESSING COMPLETED FOR L13
PROCESSING COMPLETED FOR L9
L14           11 DUP REM L13 L9 (0 DUPLICATES REMOVED)
                 ANSWERS '1-7' FROM FILE HCAPLUS
                 ANSWERS '8-11' FROM FILE BIOSIS

=> d l14 ibib abs 1-7

L14  ANSWER 1 OF 11  HCAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2003:796707  HCAPLUS
DOCUMENT NUMBER:          139:307789
TITLE:                    Preparation of imidazopyridopyrimidines as
                          inhibitors of p-38 kinase
INVENTOR(S):              Goldstein, David Michael; Hawley, Ronald
                          Charles; Lui, Alfred Sui-ting; Sjogren, Eric Brian
PATENT ASSIGNEE(S):       F. Hoffmann-La Roche Ag, Switz.
SOURCE:                   PCT Int. Appl., 61 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
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     WO 2003082871      A1   20031009       WO 2003-EP3178   20030327
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,
             UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
             CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,
             NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
             GW, ML, MR, NE, SN, TD, TG
     US 2003232847      A1   20031218       US 2003-406364   20030403
PRIORITY APPLN. INFO.:                     US 2002-369929P  P  20020403
OTHER SOURCE(S):          MARPAT 139:307789
GI
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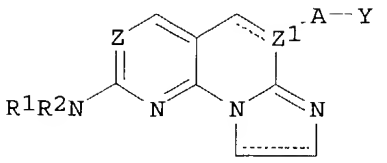

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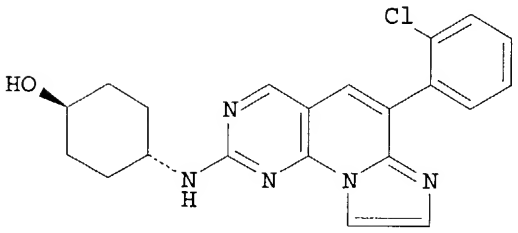

II

AB Title compds. I [Z = N, CH; Z1 = N, CH, C; R1 = H, alkyl; R2 = (un)substituted alkyl, aralkyl, cycloalkyl, heterocyclyl, aryl; A = bond, O, S, s(O), SO2, (un)substituted CH2, NH, CO; Y = alkyl, heterocyclic, (un)substituted cycloalkyl, aryl, heteroaryl] were prepared for use as inhibitors of p-38 kinase. Thus, the title compound II was prepared by treating 4-amino-2-**benzylthiopyrimidine**-5-carboxaldehyde with 2-ClC6H4CH2CN, cyclizing with ClCH2CHClOEt, oxidizing to the sulfoxide, and reaction with trans-4-aminocyclohexanol. II had IC50 for inhibition of p-38 kinase of 0.01 μM.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 2 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:738803 HCAPLUS

DOCUMENT NUMBER: 139:307697

TITLE: Design and Synthesis of 4-Azaindoles as Inhibitors of p38 MAP Kinase

AUTHOR(S): Trejo, Alejandra; Arzeno, Humberto; Browner, Michelle; Chanda, Sushmita; Cheng, Soan; Comer, Daniel D.; Dalrymple, Stacie A.; Dunten, Pete; Lafargue, JoAnn; Lovejoy, Brett; Freire-Moar, Jose; **Lim, Julie**; McIntosh, Joel; Miller, Jennifer; Papp, Eva; Reuter, Deborah; Roberts, Rick; Sanpablo, Florentino; Saunders, John; Song, Kyung; Villasenor, Armando; Warren, Stephen D.; Welch, Mary; Weller, Paul; Whiteley, Phyllis E.; Zeng, Lu; **Goldstein, David M.**

CORPORATE SOURCE: Department of Medicinal Chemistry, Roche Palo Alto LLC, Palo Alto, CA, 94304, USA

SOURCE: Journal of Medicinal Chemistry (2003), 46(22), 4702-4713
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 139:307697

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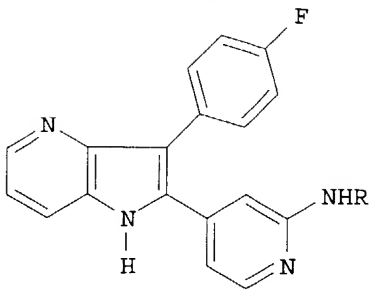

I

AB Inhibition of the biosynthesis of proinflammatory cytokines such as tumor necrosis factor and interleukin-1 via p38 has been an approach toward the development of a disease modifying agent for the treatment of chronic inflammation and autoimmune diseases. The development of a new core structure of p38 inhibitors, 3-(4-fluorophenyl)-2-(pyridin-4-yl)-1H-pyrrolo[3,2-b]pyridine, is described. X-ray crystallog. data of the lead bound to the active site of p38 was used to guide the optimization of the series. Specific focus was placed on modulating the phys. properties of the core while maintaining potent inhibition of p38. These efforts identified I [R = (R)-2-hydroxypropyl] as a potent inhibitor of p38, which also possessed the required phys. properties worthy of advanced studies.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 3 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:171896 HCAPLUS
DOCUMENT NUMBER: 136:232316
TITLE: 7-**Oxopyridopyrimidines** as inhibitors of cellular proliferation, and particularly as inhibitors of p38 kinase, for treatment of p38-related conditions
INVENTOR(S): Chen, Jian Jeffrey; Dunn, James Patrick; **Goldstein, David Michael**; **Lim, Julie Anne**
PATENT ASSIGNEE(S): F. Hoffmann-La Roche Ag, Switz.
SOURCE: PCT Int. Appl., 135 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002018380	A1	20020307	WO 2001-EP9689	20010822
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001093784	A5	20020313	AU 2001-93784	20010822
EP 1315726	A1	20030604	EP 2001-974206	20010822
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

BR 2001013628	A	20030701	BR 2001-13628		20010822
JP 2004507541	T2	20040311	JP 2002-523895		20010822
US 2002055513	A1	20020509	US 2001-943338		20010830
US 6518276	B2	20030211			
US 2002137756	A1	20020926	US 2001-943407		20010830
US 6506749	B2	20030114			
US 2003153586	A1	20030814	US 2002-230723		20020829
US 2003144307	A1	20030731	US 2002-315633		20021210

PRIORITY APPLN. INFO.:

US 2000-229584P	P	20000831
US 2000-229577P	P	20000831
WO 2001-EP9689	W	20010822
US 2001-943338	A3	20010830
US 2001-943407	A1	20010830

OTHER SOURCE(S): MARPAT 136:232316

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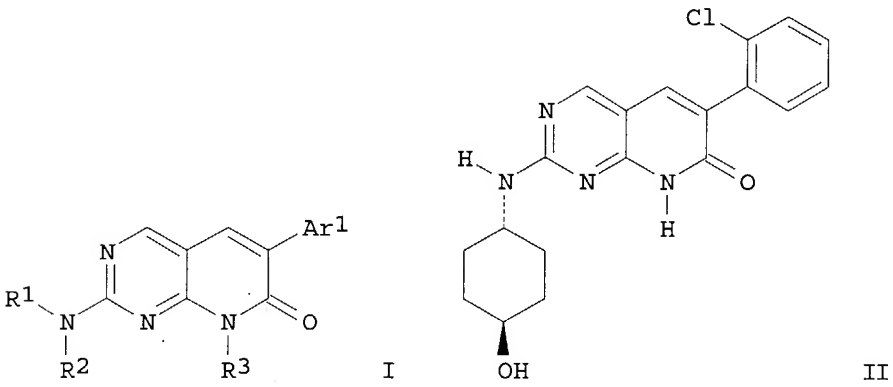

I II

AB Compds. I are disclosed [wherein: R1 = H or alkyl; R2 = substituted cycloalkyl, hetero-substituted cycloalkyl, heteroalkyl-substituted cycloalkyl, hetero-substituted cycloalkyl-aryl, heterocyclyl, heterocyclylspirocycloalkyl, aralkoxy, alkoxy, -alkylene-S(O)n-alkyl (where n = 1 or 2) or SO2Ar2; R3 = H, amino, monoalkylamino, dialkylamino, acylamino, NRaC(:O)Rb (where Ra = H or alkyl, and Rb = heterocyclyl or heteroalkyl), alkyl, cycloalkyl, aryl, aralkyl, haloalkyl, heteroalkyl, cyanoalkyl, -alkylene-C(O)R (where R = H, alkyl, OH, alkoxy, amino, monoalkylamino or dialkylamino), acyl, or phthalimidoalkyl; and each of Ar1 and Ar2 = aryl]. Also disclosed in claims is their use for treatment of disorders selected from the group consisting of arthritis, Crohn's disease, Alzheimer's disease, irritable bowel syndrome, adult respiratory distress syndrome, and chronic obstructive pulmonary disease. A list of 151 compds. I is given, as well as approx. 100 synthetic examples. For instance, cyclocondensation of 4-amino-2-(methylthio)**pyrimidine** -5-carboxaldehyde with Et (2-chlorophenyl)acetate, followed by oxidation of the sulfide to a sulfone with Oxone, and displacement of the Me sulfone with trans-4-aminocyclohexanol, gave 78% title compound II. In an in vitro p38 assay, I had IC50 values ranging from about 4.76 μM to about 0.0003 μM.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 4 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:171895 HCAPLUS

DOCUMENT NUMBER: 136:216763
TITLE: Preparation of 7-**oxopyridopyrimidines** as p38 MAP kinase inhibitors
INVENTOR(S): Arzeno, Humberto Bartolome; Chen, Jian Jeffrey; Dunn, James Patrick; **Goldstein, David Michael**; **Lim, Julie Anne**
PATENT ASSIGNEE(S): F. Hoffmann-La Roche Ag, Switz.
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002018379	A2	20020307	WO 2001-EP9688	20010822
WO 2002018379	A3	20020725		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002012147	A5	20020313	AU 2002-12147	20010822
EP 1315727	A2	20030604	EP 2001-980258	20010822
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001013590	A	20030722	BR 2001-13590	20010822
JP 2004507540	T2	20040311	JP 2002-523894	20010822
US 2002055513	A1	20020509	US 2001-943338	20010830
US 6518276	B2	20030211		
US 2003153586	A1	20030814	US 2002-230723	20020829
US 2003144307	A1	20030731	US 2002-315633	20021210

PRIORITY APPLN. INFO.:
US 2000-229577P P 20000831
US 2000-229584P P 20000831
WO 2001-EP9688 W 20010822
US 2001-943338 A3 20010830
US 2001-943407 A1 20010830

OTHER SOURCE(S): MARPAT 136:216763
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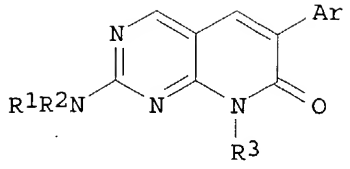

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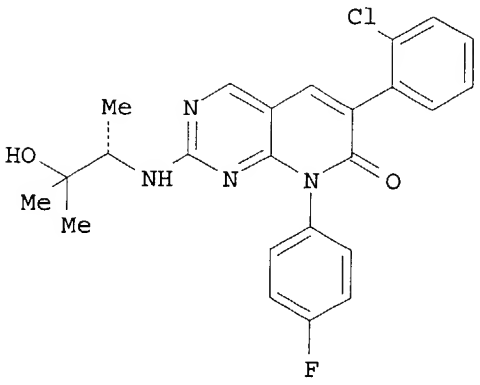

II

AB The present invention provides compds. of the formula I [R1 = H, alkyl; R2 = alkoxy-substituted alkyl, heterocyclyl, cycloalkyl; etc.; R1R2 = heterocyclyl; R3 = H, alkyl, amino, aryl, acyl, etc.; Ar = aryl], a prodrug or a pharmaceutically acceptable salt thereof, and processes for their preparation and their use for the treatment of p38 mediated disorders. Thus, II was prepared and inhibited p38 MAP kinase in vitro with IC50 of 0.0003 μM.

L14 ANSWER 5 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:300721 HCAPLUS
DOCUMENT NUMBER: 134:326540
TITLE: Preparation of alkylamino substituted bicyclic nitrogen heterocycles for pharmaceutical use as inhibitors of p38 protein kinase
INVENTOR(S): Dunn, James Patrick; Fisher, Lawrence Emerson; **Goldstein, David Michael**; Harris, William; Hill, Christopher Huw; Smith, Ian Edward David; Welch, Teresa Rosanne
PATENT ASSIGNEE(S): F. Hoffmann-La Roche Ag, Switz.
SOURCE: PCT Int. Appl., 177 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001029042	A1	20010426	WO 2000-EP10088	20001013
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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BR 2000015243	A	20020716	BR 2000-15243	20001013
EP 1228070	A1	20020807	EP 2000-967864	20001013
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				

JP 2003512378	T2	20030402	JP 2001-531840		20001013
NZ 518119	A	20040227	NZ 2000-518119		20001013
US 6451804	B1	20020917	US 2000-693337		20001020
NO 2002001781	A	20020418	NO 2002-1781		20020416
PRIORITY APPLN. INFO.:			US 1999-160803P	P	19991021
			US 2000-213743P	P	20000622
			WO 2000-EP10088	W	20001013

OTHER SOURCE(S): MARPAT 134:326540
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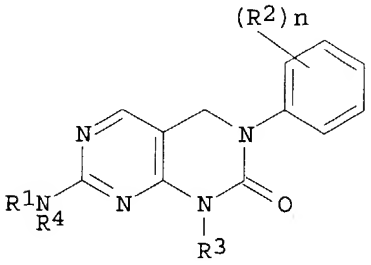

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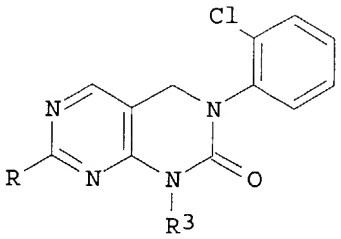


II

AB Alkylamino-substituted dihydropyrimido[4,5-d]**pyrimidinone** derivs., such as I [R1 = H, alkyl, alkenyl, alkynyl, acyl, cycloalkyl, etc.; R2 = vinyl, alkyl, halogen, heteroalkyl; R3 = alkyl, heteroalkyl, cycloalkyl, heterocyclyl, etc.; R4 = H, alkyl, etc.; n = 0-3], were prepared for pharmaceutical use. The compds. are p38 inhibitors and may be used in the treatment of arthritis, Crohn's disease, irritable bowel syndrome, adult respiratory distress syndrome, chronic obstructive pulmonary disease, osteoporosis, or Alzheimer's disease. Thus, dihydropyrimido[4,5-d]**pyrimidinone** II (R = NHCMe2CH2OH, R3 = Me) was prepared via a substitution reaction of H2NCMe2CH2OH with sulfone II (R = SO2Me, R3 = Me) when combined and heated to 100-110° for 1 h. The prepared dihydropyrimido[4,5-d]**pyrimidinone** derivs. showed 50% p38 inhibitory activity at concns. < 10 μM.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 6 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:300720 HCAPLUS
DOCUMENT NUMBER: 134:311223
TITLE: Preparation of alkylamino substituted bicyclic nitrogen heterocycles for pharmaceutical use as inhibitors of p38 protein kinase
INVENTOR(S): Dunn, James Patrick; **Goldstein, David Michael**; Harris, William; Smith, Ian Edward David; Welch, Teresa Rosanne
PATENT ASSIGNEE(S): F. Hoffmann-La Roche Ag, Switz.
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001029041	A1	20010426	WO 2000-EP10077	20001013

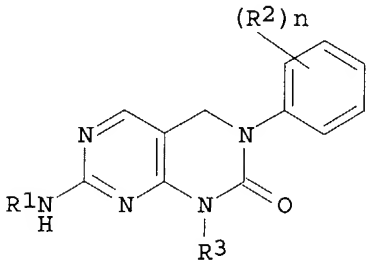
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

BR 2000014973	A	20020716	BR 2000-14973	20001013
EP 1226144	A1	20020731	EP 2000-972755	20001013
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003512377	T2	20030402	JP 2001-531839	20001013
US 6642241	B1	20031104	US 2000-693364	20001020
NO 2002001783	A	20020416	NO 2002-1783	20020416

PRIORITY APPLN. INFO.: US 1999-160804P P 19991021
US 2000-213718P P 20000622
WO 2000-EP10077 W 20001013

OTHER SOURCE(S): MARPAT 134:311223

GI



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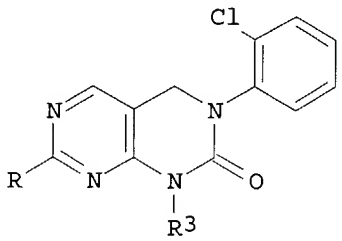


II

AB Alkylamino-substituted dihydropyrimido[4,5-d]**pyrimidinone** derivs., such as I [R1 = H, alkyl, alkenyl, alkynyl, acyl, cycloalkyl, etc.; R2 = vinyl, alkyl, halogen, heteroalkyl; R3 = alkyl, heteroalkyl, cycloalkyl, heterocyclyl, etc.; n = 0-3], were prepared for pharmaceutical use as inhibitors of p38 protein kinase for the treatment of conditions such as arthritis, Crohn's disease, obstructive pulmonary disease, or irritable bowel syndrome.. Thus, dihydropyrimido[4,5-d] **pyrimidinone** II (R = NHCHMe2, R3 = CH2CO2H) was prepared via a substitution reaction of H2NCHMe2 with sulfone II (R = SO2CH2Ph, R3 = CH2CO2Et) when combined and heated to 90-100° for 1 h. The prepared dihydropyrimido[4,5-d]**pyrimidinone** derivs. showed p38 50% inhibitory activity at concns. < 10 μM.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

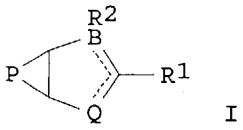
L14 ANSWER 7 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:282215 HCAPLUS
DOCUMENT NUMBER: 130:325138
TITLE: Preparation of pyrrolopyridines, furopyridines, and related compounds as p-38 MAP kinase inhibitors.
INVENTOR(S): Cheng, Soan; **Goldstein, David Michael**; Martin, Teresa Alejandra Trejo; Sjogren, Eric Brian
PATENT ASSIGNEE(S): F.Hoffmann-La Roche A.-G., Switz.
SOURCE: PCT Int. Appl., 152 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9920624	A1	19990429	WO 1998-EP6472	19981013
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2306870	AA	19990429	CA 1998-2306870	19981013
AU 9897499	A1	19990510	AU 1998-97499	19981013
AU 745579	B2	20020321		
TR 200001079	T2	20000721	TR 2000-20000107919981013	
BR 9812944	A	20000808	BR 1998-12944	19981013
EP 1025102	A1	20000809	EP 1998-951516	19981013
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2001520227	T2	20011030	JP 2000-516966	19981013
RU 2219178	C2	20031220	RU 2000-110738	19981013
US 6316464	B1	20011113	US 1998-174299	19981016
ZA 9809529	A	19990420	ZA 1998-9529	19981019
HR 2000000209	A1	20010430	HR 2000-209	20000412
NO 2000001940	A	20000413	NO 2000-1940	20000413
US 2001044538	A1	20011122	US 2001-839712	20010419
US 6479507	B2	20021112		
US 2002013354	A1	20020131	US 2001-839710	20010419
US 6630485	B2	20031007		
US 2003139462	A1	20030724	US 2002-245906	20020917

PRIORITY APPLN. INFO.:
US 1997-62548P P 19971020
US 1998-75515P P 19980220
US 1998-96916P P 19980818
WO 1998-EP6472 W 19981013
US 1998-174299 A3 19981016
US 2001-839712 A1 20010419

OTHER SOURCE(S): MARPAT 130:325138
GI



I

AB Title compds. [I; R1 = heteroaryl; when the dotted line is a double bond between Q and CR1, then B = N, R2 = aryl, and Q = CR; R = H, alkyl, haloalkyl, cycloalkyl, NO2, cyano, amino, acylamino, etc.; when the dotted line = double bond between B and CR1, then B = C; R2 = aryl, heteroaryl; Q = imino, O, S; P = atoms to form (substituted) pyrido, pyridazino, **pyrimidino**, pyrazino rings], were prepared Thus, Me isonicotinate

and 4-fluorophenylacetonitrile in EtOH were added to a solution prepared from EtOH and Na metal followed by 3 h reflux to give 2-(4-fluorophenyl)-1-(pyridin-4-yl)ethanone. The latter was azeotroped with 3-amino-2-chloropyridine and p-TsOH in PhMe to give (2-chloropyridin-3-yl)-[2-(4-fluorophenyl)-1-(pyridin-4-yl)vinyl]amine. This was heated with DABCO and (Ph3P)2PdCl2 in DMF to give 3-(4-fluorophenyl)-2-(pyridin-4-yl)-1H-pyrrolo[3,2-b]pyridine. Tested I inhibited p-38 kinase with IC50 = 68-246 nM.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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YOU HAVE REQUESTED DATA FROM 4 ANSWERS - CONTINUE? Y/(N):y

L14 ANSWER 8 OF 11 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:584809 BIOSIS
DOCUMENT NUMBER: PREV200300586852
TITLE: Alkylamino-substituted bicyclic nitrogen heterocycles.
AUTHOR(S): Dunn, James Patrick [Inventor, Reprint Author]; **Goldstein, David Michael** [Inventor]; Harris, William [Inventor]; Smith, Ian Edward David [Inventor]; Welch, Teresa Rosanne [Inventor]
CORPORATE SOURCE: Bedfordshire, UK
ASSIGNEE: Syntex (U.S.A.) LLC
PATENT INFORMATION: US 6642241 November 04, 2003
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Nov 4 2003) Vol. 1276, No. 1. http://www.uspto.gov/web/menu/patdata.html. e-file. ISSN: 0098-1133 (ISSN print).
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Dec 2003
Last Updated on STN: 10 Dec 2003
AB Alkylamino-substituted dihydropyrimido[4,5-d]**pyrimidinone** derivatives are provided which are useful as inhibitors of p38, along with a process for their manufacture and pharmaceutical preparations containing them.

L14 ANSWER 9 OF 11 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:130473 BIOSIS
DOCUMENT NUMBER: PREV200300130473
TITLE: 7-oxo-**pyridopyrimidines** (II).
AUTHOR(S): Arzeno, Humberto Bartolome [Inventor, Reprint Author]; Chen, Jian Jeffrey [Inventor]; Dunn, James Patrick [Inventor]; **Goldstein, David Michael** [Inventor]; **Lim, Julie Anne** [Inventor]
CORPORATE SOURCE: Cupertino, CA, USA
ASSIGNEE: Syntex (U.S.A.) LLC
PATENT INFORMATION: US 6518276 February 11, 2003
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Feb 11 2003) Vol. 1267, No. 2. http://www.uspto.gov/web/menu/patdata.html. e-file. ISSN: 0098-1133 (ISSN print).
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 5 Mar 2003
Last Updated on STN: 5 Mar 2003
AB The present invention provides compounds of the formula: ##STR1## wherein R1, R3, and Ar1 are those defined herein, and R2 is --CR'R"--Ra (where R'

and R" are hydrogen, hydroxyalkyl or alkyl with at least one being alkyl or hydroxyalkyl and Ra is hydroxyalkyl), Rx --S--Ry -- (where Rx is alkyl and Ry is alkylene), alkoxy-substituted alkyl, heterocyclylalkyl or C4 -C5 cycloalkyl, wherein each of the hydroxy group present in R2 can be independently Ra --C(dbdO)--O, Ra Rb N--C(dbdO)--O, or Ra --S(O)2 --O--, wherein Ra and Rb are independently hydrogen, alkyl, aryl, or aralkyl, and methods for preparation and uses thereof.

L14 ANSWER 10 OF 11 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:98140 BIOSIS
DOCUMENT NUMBER: PREV200300098140
TITLE: 7-oxo-**pyridopyrimidines** (I).
AUTHOR(S): Chen, Jian Jeffrey [Inventor, Reprint Author]; Dunn, James Patrick [Inventor]; **Goldstein, David Michael** [Inventor]; **Lim, Julie Anne** [Inventor]
CORPORATE SOURCE: San Mateo, CA, USA
ASSIGNEE: Syntex (U.S.A.) LLC
PATENT INFORMATION: US 6506749 January 14, 2003
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Jan 14 2003) Vol. 1266, No. 2. http://www.uspto.gov/web/menu/patdata.html. e-file. ISSN: 0098-1133 (ISSN print).
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 12 Feb 2003
Last Updated on STN: 12 Feb 2003

AB The present invention provides compounds of the formula: ##STR1## wherein R2 is substituted cycloalkyl, heterosubstituted cycloalkyl, heteroalkylsubstituted cycloalkyl, heterosubstituted cycloalkyl-alkyl, optionally substituted heterocyclyl, spiro-substituted cycloalkyl, aralkoxy, alkoxy, -alkylene-S(O)n -alkyl (wherein n is 1 or 2), or --SO2 Ar2 ; and R1, R3, and Ar1 are those defined herein, and methods for preparation and uses thereof.

L14 ANSWER 11 OF 11 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1999:174046 BIOSIS
DOCUMENT NUMBER: PREV199900174046
TITLE: **Pyrimidine** acyclonucleoside derivatives.
AUTHOR(S): Kim, D-K. [Inventor]; Gam, J. [Inventor]; Kim, G. [Inventor]; Kim, Y-W. [Inventor]; Lee, N. [Inventor]; **Lim, J.** [Inventor]; Kim, H-T. [Inventor]; Kim, K. H. [Inventor]
CORPORATE SOURCE: Seoul, North Korea
ASSIGNEE: SUNKYONG INDUSTRIES CO., INC.
PATENT INFORMATION: US 5889013 March 30, 1999
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (March 30, 1999) Vol. 1220, No. 5, pp. 4591. print. CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 5 May 1999
Last Updated on STN: 5 May 1999

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AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: May 7, 2004 (20040507/UP).

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